## REMARKS

Claims 22-34 are pending in the present application and at issue. Claims 22, 24 and 34 have been amended to address the indefiniteness rejection.

It is respectfully submitted that the present amendment presents no new issues or new matter and places this case in condition for allowance. Reconsideration of the application in view of the above amendments and the following remarks is requested.

### I. The Objection to the Specification

The Office objected to the specification because sequences are recited in the drawings, which are not identified by their corresponding sequence identifiers. Applicants will amend the Brief Description of the Figures upon an indication of allowable subject matter.

### II. The Rejection of Claims 22-28 under 35 U.S.C. 112

Claims 22-28 are rejected under 35 U.S.C. 112 as failing to comply with the written description requirement. This rejection is respectfully traversed.

As set forth in Federal Circuit decisions, a specification complies with the written description requirement if it provides "a precise definition, such as by structure, formula, chemical name, or physical properties of the claimed subject matter sufficient to distinguish it from other materials." See, e.g., *University of California v. Eli Lilly and Co.*, 43 U.S.P.Q.2d 1398, 1404 (Fed. Cir. 1997); *Enzo Biochem v. Gen-Probe Inc.*, 63 U.S.P.Q.2d 1609, 1613 (Fed. Cir. 2002).

The claimed invention is drawn to protein variants having reduced immunogenicity as compared with its wild-type protein, wherein the amino acid sequence of the protein variant differs from the amino acid sequence of the wild-type protein with respect to at least one epitope area of the wild-type protein. The specification contains an extensive disclosure of wild-type proteins from which the protein variants of the present invention are derived.

Based on Applicants' disclosure, the skilled artisan would be led to make other protein variants to obtain the benefits described in the present application. Applicants therefore submit that the specification demonstrates that Applicants had possession of the claimed invention at the time the application was filed.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 112. Applicants respectfully request reconsideration and withdrawal of the rejection.

**III. The Rejection of Claims 22-28 under 35 U.S.C. 112**

Claims 22-28 are rejected under 35 U.S.C. 112 for failing to comply with the enablement requirement. This rejection is respectfully traversed.

It is well settled that an assertion by the Patent Office that the enabling disclosure is not commensurate in scope with the protection sought must be supported by evidence or reasoning substantiating the doubts so expressed. *In re Dinh-Nguyen*, 181 U.S.P.Q. 46 (C.C.P.A. 1974). See also *U.S. v. Telectronics*, 8 U.S.P.Q.2d 1217 (Fed. Cir. 1988); *In re Bowen*, 181 U.S.P.Q. 48 (C.C.P.A. 1974); *Ex parte Hitzeman*, 9 U.S.P.Q.2d 1821 (BPAI 1988).

Moreover, in the absence of any evidence or apparent reason why compounds do not possess the disclosed utility, the allegation of utility in the specification must be accepted as correct. *In re Kamal*, 158 U.S.P.Q. 320 (C.C.P.A. 1968). See also *In re Stark*, 172 U.S.P.Q. 402, 406 n. 4 (C.C.P.A. 1972) (the burden is upon the Patent Office to set forth reasonable grounds in support of its contention that a claim reads on inoperable subject matter).

Applicants submit that the specification complies with the enablement requirement.

The claimed inventions are drawn to protein variants having reduced immunogenicity as compared with its wild-type protein, wherein the amino acid sequence of the protein variant differs from the amino acid sequence of the wild-type protein with respect to at least one epitope area of the wild-type protein. As explained above, the specification contains an extensive disclosure of wild-type proteins from which the protein variants are derived.

Based on Applicants' disclosure, the skilled artisan would be led to make other protein variants to obtain the benefits described in the present application. Applicants therefore submit that the specification enables the protein variants of the present invention.

We draw the Examiner's attention to *In re Angstadt*, 190 U.S.P.Q. 214 (C.C.P.A. 1976). In *Angstadt*, the claimed process of preparing hydroperoxides used a metal salt complex as a catalyst. The specification disclosed catalysts that worked and some that gave little or no yield of hydroperoxides. The claims were rejected for lack of enablement, specifically as requiring undue experimentation to find useful catalysts. This rejection was reversed by the CCPA.

In holding that the claims did satisfy 35 USC 112, the Court observed, 190 U.S.P.Q. at 218:

> We cannot agree with the board that appellants' disclosure is not sufficient to enable one of ordinary skill in the art to practice the invention without undue experimentation. We note that many chemical processes, and catalytic processes particularly, are unpredictable, [citation omitted] and that the scope of enablement varies inversely with the degree of unpredictability involved, [citation

> omitted]. That this particular process is unpredictable is demonstrated further by appellants in their specification. Appellants have disclosed forty examples: one of these examples yields no hydroperoxides in the final product. Also, appellants have expressly indicated in their specification that some of these organometallic complex catalysts 'yield *** no hydroperoxides in the final product.'
>
> Appellants have apparently not disclosed every catalyst which will work; they have apparently not disclosed every catalyst which will not work. The question, then, is whether in an unpredictable art, section 112 requires disclosure of a test with every species covered by a claim. To require such a complete disclosure would apparently necessitate a patent application or applications with 'thousands' of catalysts along with information as to whether each exhibits catalytic behavior resulting in the production of hydroperoxides. More importantly, such a requirement would force an inventor seeking adequate patent protection to carry out a prohibitive number of actual experiments. This would tend to discourage inventors from filing patent applications in an unpredictable area since the patent claims would have to be limited to those embodiments which are expressly disclosed. A potential infringer could readily avoid 'literal' infringement of such claims by merely finding another analogous catalyst complex which could be used in 'forming hydroperoxides.'

This admonition applies with equal force to the present application, which describes numerous protein variants of the present invention. To require more would fly in the face of the *Angstadt* holding.

The Court, 190 USPQ at 218, recognized that some experimentation might be necessary for the skilled worker to select non-exemplified catalysts for use:

> Appellants have, in effect, provided those skilled in this art with a large but finite list of transition metal salts from which to choose in preparing such a complex catalyst. Appellants have actually carried out 40 runs using various transition metal salts and hexaalkylphosphoramides. If one skilled in this art wished to make and use a transition metal salt other than those disclosed in appellants' 40 runs, he would merely read appellants' specification for directions how to make and use the catalyst complex to oxidize the alkylaromatic hydrocarbons, and could then determine whether hydroperoxides are, in fact, formed. The process discovered by appellants is not complicated, and there is no indication that special equipment or unusual reaction conditions must be provided when practicing the invention. One skilled in this art would merely have to substitute the correct mass of a transition metal salt for the transition metal salts disclosed in appellants' 40 runs. Thus, we have no basis for concluding that persons skilled in this art, armed with the specification and its 40 working examples, would not easily be able to determine which catalyst complexes within the scope of the claims work to produce hydroperoxides and which do not.

However, while some experimentation might be necessary, as long as the experimentation was not "undue experimentation," the claims would not violate 35 USC 112, *Angstadt*, Id:

> Since appellants have supplied the list of catalysts and have taught how to make and how to use them, we believe that the experimentation required to determine which catalysts will produce hydroperoxides would not be undue and certainly would not 'require ingenuity beyond that to be expected of one of ordinary skill in the art.' (Emphasis added).

As in *Angstadt*, the present application discloses numerous parent proteins and protein variants of the present invention. While some experimentation might be necessary to identify other non-exemplified protein variants, such experimentation would require carrying out a simple process without special equipment or unusual reaction conditions, as in *Angstadt*. This experimentation, if required, "would not be undue and certainly would not 'require ingenuity beyond that expected of one of ordinary skill in the art.'" (*Angstadt*, 190 U.S.P.Q. at 218). Certainly, there is no evidence of record to the contrary.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 112. Applicants respectfully request reconsideration and withdrawal of the rejection.

**IV. The Rejection of Claims 22-28 under 35 U.S.C. 112**

Claims 22-28 are rejected under 35 U.S.C. 112 as being indefinite. Claims 22, 24 and 34 are amended to address this rejection. Applicants therefore submit that this rejection has been overcome.

**V. The Rejection of Claims 22-26 and 28 under 35 U.S.C. 102**

Claims 22-26 and 28 are rejected under 35 U.S.C. 102 as being anticipated by Lovborg et al. (WO 92/10755). This rejection is respectfully traversed.

Lovborg discloses protein variants that are randomly constructed, which are then evaluated for lower immunogenicity relative to the parent protein. Once protein variants that have lower immunogenicity are identified, Lovborg determines the epitope.

However, Lovborg do not disclose the protein variants of the present invention.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 102. Applicants respectfully request reconsideration and withdrawal of the rejection.

## VI. The Rejection of Claims 22-26 and 28 under the Doctrine of Obviousness-Type Double Patenting

Claims 22-26 and 28 are rejected under the doctrine of obviousness-type double patenting as being unpatentable over claims 22-24 and 26-29 of copending U.S. Application No. 09/957,806.

Applicants will file a terminal disclaimer upon an indication of allowable subject matter.

## VII. Conclusion

In view of the above, it is respectfully submitted that all claims are in condition for allowance. Early action to that end is respectfully requested. The Examiner is hereby invited to contact the undersigned by telephone if there are any questions concerning this amendment or application.

Respectfully submitted,

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